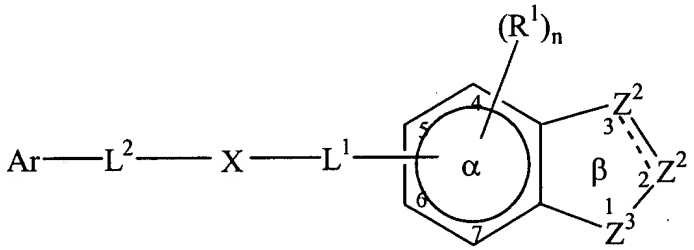
CLAIM AMENDMENTS

1. (currently amended): A compound of the formula:

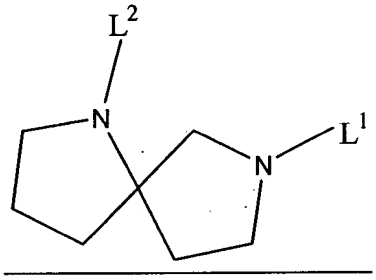


(1)

and the pharmaceutically acceptable salts thereof~~, or a pharmaceutical composition thereof,~~ wherein:

Ar is an aryl group substituted with 0-5 non-interfering substituents, wherein two adjacent noninterfering substituents can form a fused aromatic or nonaromatic ring;

L^2-X-L^1 is of the formula:



L^1 and L^2 are linkers;

~~X is an aliphatic monocyclic or aliphatic polycyclic moiety optionally comprising one or more hetero ring atoms wherein the cyclic moiety may be optionally substituted with one or more noninterfering substituents and where said optional substituents may constitute a ring fused to X;~~

n is 0-3;

each R^1 is hydrogen or a noninterfering substituent;

 represents a single or double bond;

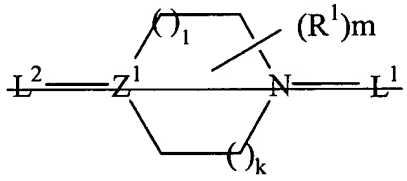
one Z^2 is CA or CR^2A; the other Z^2 is CR^3, CR^3_2, NR^4 or N; and each R^2, R^3 and R^4 is independently hydrogen or a noninterfering substituent;

Z^3 is NR^5 or O; where R^5 is hydrogen or a noninterfering substituent;

A is $-W_i-COX_jY$, where Y is COR^6 or an isostere thereof, each of W and X is a spacer of 2-6Å; each of i and j is independently 0 or 1; and R^6 is a noninterfering substituent~~;~~

~~and wherein the smallest number of covalent bonds in the compound separating the atom of Ar linked to L^2 and the atom of the α ring linked to L^1 is at least 5, each said bond having a bond length of 1.2 to 2.0 angstroms; and/or the distance in space between the atom of Ar linked to L^2 and the atom of the α ring linked to L^1 is 4.5—24 angstroms;~~

~~and with the proviso that the portion of the compound represented by L^2-X-L^1 is not:~~



~~where L^2 and L^1 are linkers; Z^1 is CR or N wherein R is hydrogen or a non-interfering substituent; each R^1 is independently a non-interfering substituent; and each of l and k is 0-3; and m is 0-4.~~

2. (original): The compound of claim 1 wherein A is $COXjCOR^6$, and

wherein R^6 is H, or is straight or branched chain alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroalkyl, heteroaryl, or heteroarylalkyl, each optionally substituted with halo, alkyl, heteroalkyl, SR, SOR, SO_2R, SO_2NR_2, OR, NR_2, OCOR, NRCOR, $NRCONR_2$, $NRSO_2R$, $NRSO_2NR_2$, $OCONR_2$, CN, COOR, $CONR_2$, COR, or R_3Si wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof, or

wherein R^6 is OR, NR_2, SR, $NRCONR_2$, $OCONR_2$, or $NRSO_2NR_2$, wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof, and wherein two R attached to the same atom may form a 3-8 member carbocyclic or heterocyclic ring and wherein said ring may further be substituted by alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroalkyl, heteroaryl, heteroarylalkyl, each optionally substituted with halo, SR, OR, NR_2, OCOR, NRCOR, $NRCONR_2$, $NRSO_2R$, $NRSO_2NR_2$, $OCONR_2$, or R_3Si wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof wherein two R attached to the same atom may form a 3-8 member ring, optionally substituted as above defined; and

X, if present, is CR_2, wherein R is independently H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof wherein two R attached to the same atom may form a 3-8 member ring, optionally substituted as above defined.

3. (original): The compound of claim 1 wherein Y is an isostere of COR^6.

4. (original): The compound of claim 3 wherein Y is tetrazole; 1,2,3-triazole; 1,2,4-triazole; or imidazole.

5. (original): The compound of claim 1 wherein each of i and j is 0.

6. (original): The compound of claim 2 wherein j is 0.

7. (original): The compound of claim 1 wherein Z^3 is NR^5.

8. (original): The compound of claim 7 wherein R^5 is H or is optionally substituted alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, or is SOR, SO_2R, RCO, COOR, alkyl-COR, SO_3R, $CONR_2$, SO_2NR_2, CN, CF_3, NR_2, OR, alkyl-SR, alkyl-SOR, alkyl-SO_2R, alkyl-OCOR, alkyl-COOR, alkyl-CN, alkyl-$CONR_2$, or R_3Si, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof.

9. (original): The compound of claim 8 wherein R^5 is H, or is optionally substituted alkyl or acyl.

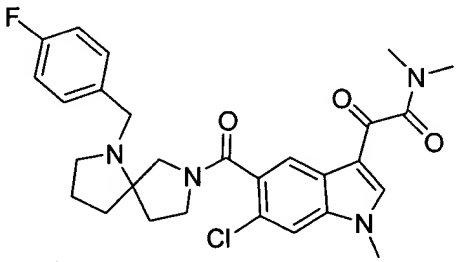
10. (canceled)

11. (currently amended): The compound of claim [[10]] 1 wherein R^2 and R^3 are independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR, NR_2, SR, SOR, SO_2R, OCOR, NRCOR, $NRCONR_2$, NRCOOR, $OCONR_2$, RCO, COOR, alkyl-OOR, SO_3R, $CONR_2$, SO_2NR_2, $NRSO_2NR_2$, CN, CF_3, R_3Si, and NO_2, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof and two of R^2 and/or R^3 on adjacent positions can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members, or R^2 and/or R^3 is =O or an oxime, oximeether, oximeester or ketal thereof.

12. (original): The compound of claim 11 wherein R^2 and R^3 are independently selected from halo, OR and alkyl.

13-38. (canceled)

39. (currently amended): The compound of claim [[38]] 1 wherein the compound is:



40. (original): The compound of claim 1 wherein L^1 and L^2 are independently selected from CO, CHOH, CH_2-NH-CO, CH_2-N-CH3, and CH_2.

41. (original): The compound of claim 40 wherein L^1 and/or L^2 is CO.

42. (original): The compound of claim 41 wherein L^1 and/or L^2 is CH_2-NH-CO.

43. (currently amended): The compound of claim 41 wherein L^1 and/or L^2 is ~~CH_2-N-CH3~~ CH_2-N-CH_2.

44. (currently amended): The compound of claim 1 wherein L^2 is alkylene (1-4C), alkenylene ~~(1-4C)~~ (2-4C), heteroalkylene (1-4C) or ~~hetero-alkyenylene~~ heteroalkenylene, wherein the foregoing are optionally substituted with a moiety selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR, NR_2, SR, SOR, SO_2R, OCOR, NRCOR, $NRCONR_2$, NRCOOR, $OCONR_2$, RCO, COOR, alkyl-OOR, SO_3R, $CONR_2$, SO_2NR_2, $NRSO_2NR_2$, CN, CF_3, R_3Si, and NO_2, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof, and wherein two substituents on L^2 can be joined to form a non-aromatic saturated or unsaturated ring that includes 0-3 heteroatoms which are O, S and/or N and which

contains 3 to 8 members or said two substituents can be joined to form a carbonyl moiety or an oxime, oximeether, oximeester or ketal of said carbonyl moiety.

45. (original): The compound of claim 44 wherein L^2 and/or L^1 is unsubstituted alkylene.

46. (currently amended): The compound of claim 44 wherein L^2 and/or L^1 is unsubstituted methylene, or methylene substituted with alkyl~~, or -CH=~~.

47. (original): The compound of claim 1 wherein Ar is optionally substituted with 0-5 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR, NR_2, SR, SOR, SO_2R, OCOR, NRCOR, $NRCONR_2$, NRCOOR, $OCONR_2$, RCO, COOR, alkyl-OOR, SO_3R, $CONR_2$, SO_2NR_2, $NRSO_2NR_2$, CN, CF_3, R_3Si, and NO_2, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof, and wherein two of said optional substituents on adjacent positions can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members.

48. (original): The compound of claim 47 wherein Ar is optionally substituted phenyl.

49. (original): The compound of claim 48 wherein said optional substitution is by halo, OR, or alkyl.

50. (original): The compound of claim 49 wherein said phenyl is unsubstituted or has a single substituent.

51. (original): The compound of claim 1 wherein each R^1 is halo, alkyl, heteroalkyl, OCOR, OR, NRCOR, SR, or NR_2, wherein R is H, alkyl, aryl, or heteroforms thereof.

52. (original): The compound of claim 51 wherein R^1 is halo or alkoxy.

53. (original): The compound of claim 52 wherein n is 0, 1 or 2.

54. (original): The compound of claim 1 wherein L^1 is coupled to the α ring at the 4-, 5- or 6-position.

55. (original): The compound of claim 1 wherein Z^2 at position 3 is CA or CHA.

56. (original): The compound of claim 55 wherein the Z^2 at position 2 is CR^3 or CR^3_2.

57. (original): The compound of claim 56 wherein R^3 is hydrogen, or is alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR, NR_2, SR, SOR, SO_2R, OCOR, NRCOR, $NRCONR_2$, NRCOOR, $OCONR_2$, RCO, COOR, alkyl-OOR, SO_3R, $CONR_2$, SO_2NR_2, $NRSO_2NR_2$, CN, CF_3, R_3Si, and NO_2, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof and two of R^1 can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members.

58. (original): The compound of claim 57 wherein each R^3 is selected from the group consisting of H, alkyl, acyl, aryl, arylalkyl, heteroalkyl, heteroaryl, halo, OR, NR_2, SR, NRCOR, alkyl-OOR, RCO, COOR, and CN, wherein each R is independently H, alkyl, or aryl or heteroforms thereof.

59. (original): The compound of claim 55 wherein Z^2 at position 2 is N or NR^4.

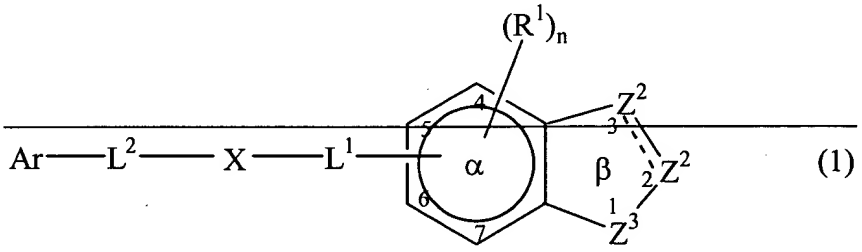
60. (original): The compound of claim 59 wherein R^4 is H, or alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, or is SOR, SO_2R, RCO, COOR, alkyl-COR, SO_3R, $CONR_2$, SO_2NR_2, CN, CF_3, or R_3Si wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof.

61. (original): The compound of claim 1 wherein  represents a double bond.

62. (canceled)

63. (currently amended): A pharmaceutical composition for treating conditions characterized by enhanced p38-α activity which composition comprises

a therapeutically effective amount of a compound of claim 1 and a pharmaceutically acceptable excipient ~~the formula~~



~~and the pharmaceutically acceptable salts thereof, or a pharmaceutical composition thereof, wherein~~

~~Ar is an aryl group substituted with 0-5 non-interfering substituents, wherein two adjacent noninterfering substituents can form a fused aromatic or nonaromatic ring;~~

~~L^1 and L^2 are linkers;~~

~~X is an aliphatic monocyclic or aliphatic polycyclic moiety optionally comprising one or more hetero ring atoms wherein the cyclic moiety may be optionally substituted with one or more noninterfering substituents and where said optional substituents may constitute a ring fused to X;~~

~~n is 0-3;~~

~~each R^1 is hydrogen or a noninterfering substituent;~~

~~represents a single or double bond;~~

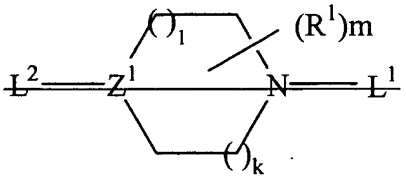
~~one Z^2 is CA or CR^2A; the other Z^2 is CR^3, CR^3_2, NR^4 or N; and each R^2, R^3 and R^4 is independently hydrogen or a noninterfering substituent;~~

~~Z^3 is NR^5 or O; where R^5 is hydrogen or a noninterfering substituent;~~

~~A is $-W_i-COX_jY$, where Y is COR^6 or an isostere thereof, each of W and X is a spacer of 2-6Å; each of i and j is independently 0 or 1; and R^6 is a noninterfering substituent;~~

~~and wherein the smallest number of covalent bonds in the compound separating the atom of Ar linked to L^2 and the atom of the α ring linked to L^1 is at least 5, each said bond having a bond length of 1.2 to 2.0 angstroms; and/or the distance in space between the atom of Ar linked to L^2 and the atom of the α ring linked to L^1 is 4.5—24 angstroms;~~

~~and with the proviso that the portion of the compound represented by L^2-X-L^1 is not:~~

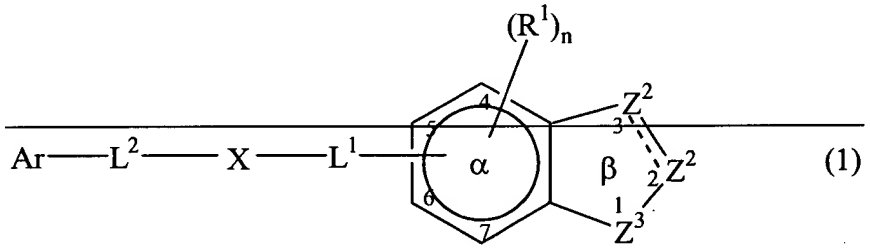


~~where L^2 and L^1 are linkers; Z^1 is CR or N wherein R is hydrogen or a non-interfering substituent; each R^1 is independently a non-interfering substituent; and each of l and k is 0-3; and m is 0-4.~~

64. (original): The composition of claim 63 which further contains an additional therapeutic agent.

65. (original): The composition of claim 64 wherein said additional therapeutic agent is a corticosteroid, a monoclonal antibody, or an inhibitor of cell division.

66. (currently amended): A method to treat a condition mediated by p38-α kinase comprising administering to a subject in need of such treatment a compound of claim 1 ~~the formula:~~



(1)

~~and the pharmaceutically acceptable salts thereof,~~ or a pharmaceutical composition thereof ~~, wherein~~

~~Ar is an aryl group substituted with 0-5 non-interfering substituents, wherein two adjacent noninterfering substituents can form a fused aromatic or nonaromatic ring;~~

~~L^1 and L^2 are linkers;~~

~~X is an aliphatic monocyclic or aliphatic polycyclic moiety optionally comprising one or more hetero ring atoms wherein the cyclic moiety may be optionally substituted with one or more noninterfering substituents and where said optional substituents may constitute a ring fused to X;~~

~~n is 0-3;~~

~~each R^1 is hydrogen or a noninterfering substituent;~~

~~--- represents a single or double bond;~~

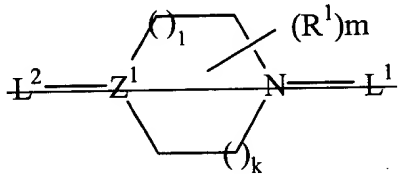
~~one Z^2 is CA or CR^2A; the other Z^2 is CR^3, CR^3_2, NR^4 or N; and each R^2, R^3 and R^4 is independently hydrogen or a noninterfering substituent;~~

~~Z^3 is NR^5 or O; where R^5 is hydrogen or a noninterfering substituent;~~

~~A is $-W_i-COX_jY$, where Y is COR^6 or an isostere thereof, each of W and X is a spacer of 2-6Å; each of i and j is independently 0 or 1; and R^6 is a noninterfering substituent;~~

~~and wherein the smallest number of covalent bonds in the compound separating the atom of Ar linked to L^2 and the atom of the α ring linked to L^1 is at least 5, each said bond having a bond length of 1.2 to 2.0 angstroms; and/or the distance in space between the atom of Ar linked to L^2 and the atom of the α ring linked to L^1 is 4.5 - 24 angstroms;~~

~~and with the proviso that the portion of the compound represented by L^2-X-L^1 is not:~~



~~where L^2 and L^1 are linkers; Z^1 is CR or N wherein R is hydrogen or a non-interfering substituent; each R^1 is independently a non-interfering substituent; and each of l and k is 0-3; and m is 0-4~~.

67. (original): The method of claim 66 wherein said condition is a proinflammation response.

68. (original): The method of claim 67 wherein said proinflammation response is multiple sclerosis, IBD, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gouty arthritis, other arthritic conditions, sepsis, septic shock, endotoxic shock, Gram-negative sepsis, toxic shock syndrome, asthma, adult respiratory distress syndrome, stroke, reperfusion injury, CNS injury, psoriasis, restenosis, cerebral malaria, chronic pulmonary inflammatory disease, silicosis, pulmonary sarcosis, a bone resorption disease, graft-versus-host reaction, Crohn's Disease, ulcerative colitis, Alzheimer's or pyresis.